

## CLAIMS

What Is Claimed Is:

1. A combinatorial library of indolinone compounds, comprising a series of at least ten indolinones that can be formed by reacting oxindoles with aldehydes.

2. The combinatorial library of claim 1 wherein said oxindoles are type A oxindoles.

3. The combinatorial library of claim 1 wherein said aldehydes are type B aldehydes.

4. The combinatorial library of claim 1 wherein said library comprises at least 100 indolinones.

5. The combinatorial library of claim 1 wherein said library comprises at least 1000 indolinones.

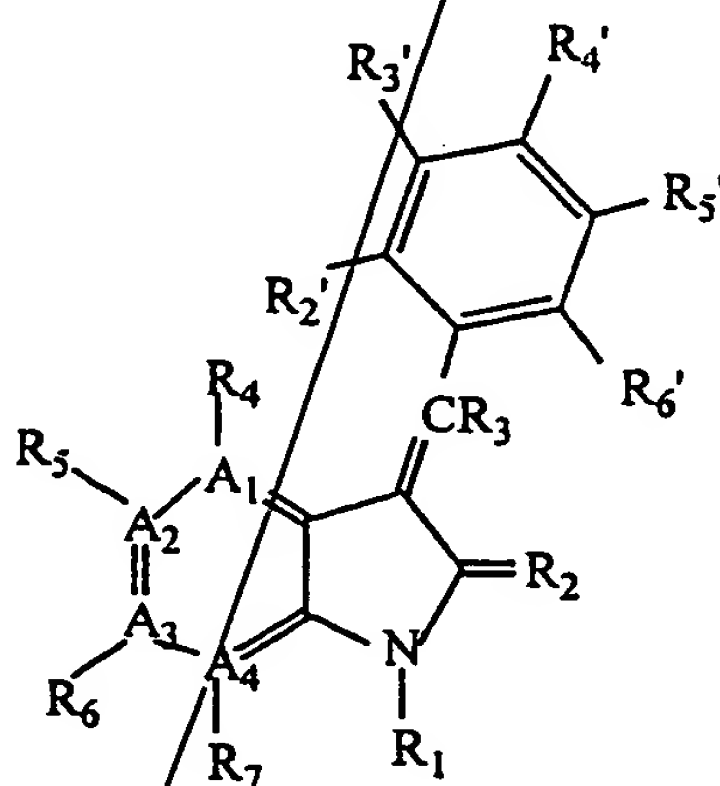
6. The combinatorial library of claim 1, wherein most of said indolinones are in the cis conformation.

7. A method of making an indolinone comprising the steps of  
(a) creating a combinatorial library of

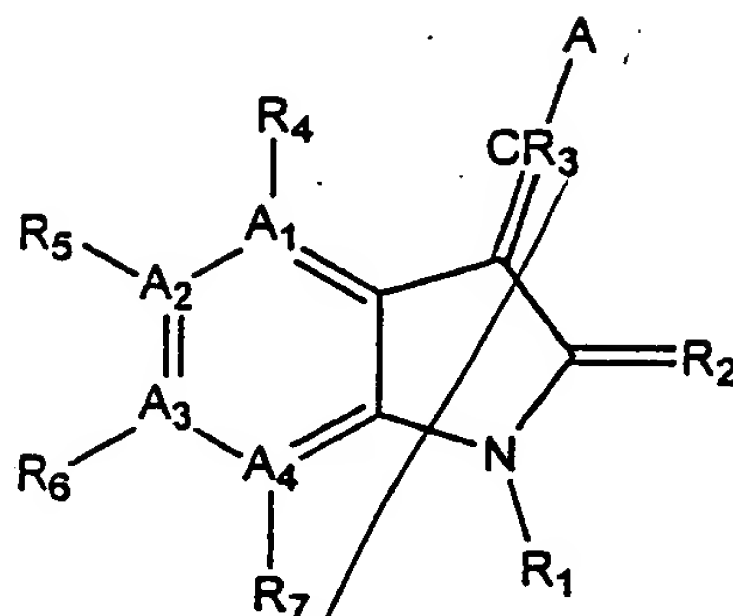
indolinones by reacting a series of  
oxindoles with a series of aldehydes,

- (b) testing said indolinones in biological assays,  
(c) selecting one or more indolinones with favorable  
activity; and  
(d) synthesizing one or more of said indolinones  
selected in step (c).

8. A compound having formula V or VI



(V)



(VI)

and pharmaceutically acceptable salts, isomers,  
 5 metabolites, esters, amides, and prodrugs thereof, wherein:

(a)  $A_1$ ,  $A_2$ ,  $A_3$ , and  $A_4$  are independently carbon or  
 nitrogen;

(b)  $R_1$  is hydrogen or alkyl;

(c)  $R_2$  is oxygen or sulfur;

(d)  $R_3$  is hydrogen;

(e)  $R_4$ ,  $R_5$ ,  $R_6$ , and  $R_7$  are optionally present and are  
 each independently selected from (i) the group consisting  
 of hydrogen, alkyl, alkoxy, aryl, aryloxy, alkaryl,  
 alkaryloxy, halogen, trihalomethyl,  $S(O)R$ ,  $SO_2NRR'$ ,  $SO_3R$ ,  
 15  $SR$ ,  $NO_2$ ,  $NRR'$ ,  $OH$ ,  $CN$ ,  $C(O)R$ ,  $OC(O)R$ ,  $NHC(O)R$ ,  $(CH_2)_nCO_2R$ ,  
 and  $CONRR'$  or (ii) any two adjacent  $R_4$ ,  $R_5$ ,  $R_6$ , and  $R_7$  taken  
 together form a fused ring with the aryl portion of the  
 oxindole-based portion of the indolinone;

(f)  $R_2'$ ,  $R_3'$ ,  $R_4'$ ,  $R_5'$ , and  $R_6'$  are each independently

selected from the group consisting of hydrogen, alkyl, alkoxy, aryl, aryloxy, alkaryl, alkaryloxy, halogen, trihalomethyl, S(O)R, SO<sub>2</sub>NRR', SO<sub>3</sub>R, SR, NO<sub>2</sub>, NRR', OH, CN, C(O)R, OC(O)R, NHC(O)R, (CH<sub>2</sub>)<sub>n</sub>CO<sub>2</sub>R, and CONRR';

- 5 (g) n is 0, 1, 2, or 3;  
(h) R is H, alkyl or aryl; and  
(i) R' is H, alkyl or aryl.

(j) A is a five membered heteroaryl ring selected from the group consisting of thiophene, pyrrole, pyrazole, imidazole, 1,2,3-triazole, 1,2,4-triazole, oxazole, isoxazole, thiazole, isothiazole, furan, 1,2,3-oxadiazole, 1,2,4-oxadiazole, 1,2,5-oxadiazole, 1,3,4-oxadiazole, 1,2,3,4-oxatriazole, 1,2,3,5-oxatriazole, 1,2,3-thiadiazole, 1,2,4-thiadiazole, 1,2,5-thiadiazole, 1,3,4-thiadiazole, 1,2,3,4-thiatriazole, 1,2,3,5-thiatriazole, and tetrazole, optionally substituted at one or more positions with alkyl, alkoxy, aryl, aryloxy, alkaryl, alkaryloxy, halogen, trihalomethyl, S(O)R, SO<sub>2</sub>NRR', SO<sub>3</sub>R, SR, NO<sub>2</sub>, NRR', OH, CN, C(O)R, OC(O)R, NHC(O)R, (CH<sub>2</sub>)<sub>n</sub>CO<sub>2</sub>R or  
15 CONRR'.  
20

9. A pharmaceutical composition comprising a pharmaceutically acceptable carrier or excipient and a compound according to Claim 8.

10. A method for treating diseases related to  
25 unregulated tyrosine kinase signal transduction, the method

comprising the step of administering to a subject in need thereof a therapeutically effective amount of a compound according to Claim 8.

11. A method for regulating tyrosine kinase  
5 signal transduction comprising administering to a subject a therapeutically effective amount of a compound according to Claim 8.

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5 signal transduction comprising administering to a subject a therapeutically effective amount of a compound according to Claim 8.